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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/194,996	09/20/1999	Jean-Luc Dubois	146.1309	3834

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Charles A Muserlian
Bierman Muserlian & Lucas
600 Third Avenue
New York, NY 10016

EXAMINER	
GHALI, ISIS A D	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 03/03/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/194,996	DUBOIS, JEAN-LUC	
	Examiner	Art Unit	
	Isis Ghali	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/04/1998*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-10 are included in the prosecution.

Specification

1. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.
(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a

nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

2. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

3. The use of the trademarks: "Vistanex", "Oppanol", "Gelva", "Acronal", "Durotak", "Eudragit", "BIO PSA", "Scotchpak", "Hoechst's Hostaphan", "Kollidon", "Premarin" and ""ST 1435" have been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

4. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Objections

5. Claims 7-10 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend on another multiple dependent claim. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the expression "rapidly covered" and the expression does not set out the metes and bounds of the claim. Recourse to the specification does not define the expression "rapidly covered". Clarification is requested.

Regarding claims 3 and 5, the claims contain the trademark/trade names "ST 1435" and "Premarin", respectively. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claims' scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods associated with the trademark or trade name. In the present case, the trademarks/trade names are used to identify/describe steroid sex hormones and, accordingly, the identification/description is indefinite.

Regarding claims 5 and 9, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 9 recites the limitation "solvent" in line 7 of the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-3, 5, 6, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,904,931 ('931).

US '931 teaches a transdermal therapeutic system for administering a mixture of steroid sex hormones (abstract; col.4, lines 2-4). The system comprises two active ingredients containing matrix layers arranged side by side wherein one matrix is loaded with gestagen and the other is loaded with estrogen (col.6, lines 1-3, 28-32; col.8, example 4). Examples of gestagens include gestodene, levonorgestrel, desogestrel, norethisterone and norethisterone acetate (col.1, lines 20-22). Examples of estrogen include estradiol (col.1, lines 27-35). The two matrices are separated by space and care must be taken for sufficient spacing of the areas to prevent a diffusion of active

ingredient in the respective other area (col.6, lines 36-39). Each matrix is covered by a separate cover layer and the system as a whole is covered by a removable protective layer (Figure 2, col.6, lines 50-57). The system is provided by skin contact adhesive layer (col.4, lines 34-35). The matrix is silicone adhesive or acrylate adhesive (col.5, lines 15-19; col.7, lines 40-43; col.8, example 4). The size of the system ranges from 1-100 cm^2 (col.5, lines 60-62). The reference further disclosed that gestagen is used with silicone adhesive and estrogen is used with polyacrylate adhesive (col.7, example 1; col.8, lines 35-38). The reference disclosed method of making the system including the steps of mixing the hormone with the adhesive and the solvent, coating the mixture on the cover layer, drying the mixture and applying the removable protective layer, and finally laminating and punching the product to obtain the individual patches (col.4, lines 49-64; col.8, example 4).

US '931 does not teach the size of the space that separate the two matrices as claimed in claim 1.

The claimed size does not impart patentability to the claims, absent evidence to the contrary. However, the reference suggests that care must be taken for sufficient spacing of the areas to prevent a diffusion of active ingredient in the respective other area.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal therapeutic system comprising two adhesive matrices, one loaded with progesterone and the other loaded with estrogen as disclosed by US '931, and adjust the space between the two matrices to obtain

independent delivery of the two hormones, motivated by the teaching of the reference that care must be taken for sufficient spacing of the areas to prevent a diffusion of active ingredient in the respective other area, with reasonable expectation of having transdermal therapeutic system that deliver progesterone and estrogen from two separate matrices to the patient in need of such treatment with success.

10. Claims 1-3, 5, 6, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,858,394 ('394).

US '394 teaches a transdermal therapeutic system for administering a mixture of steroid sex hormones (abstract; col.1, lines 41-44). The system comprises two active ingredients containing matrix layers arranged side by side wherein one matrix is loaded with gestodene and the other is loaded with estrogen (col.5, lines 11-16, 38-45; col.8, example 4). Examples of estrogen include estradiol (col.2, lines 10-12). The two matrices are separated by space and care must be taken for sufficient spacing of the areas to prevent a diffusion of active ingredient in the respective other area (col.5, lines 20-23). Each matrix is covered by a separate cover layer and the system as a whole is covered by a removable protective layer (Figure 2, col.5, lines 38-45). The system is provided by skin contact adhesive layer (col.4, lines 13-14). The matrix is silicone adhesive or acrylate adhesive (col.4, lines 16-19; col.6, lines 66-67; col.8, example 4). The size of the system ranges from 5-100 cm^2 (col.4, lines 32-33). The reference further disclosed that gestagen is used with silicone adhesive and estrogen is used with polyacrylate adhesive (col.6, example 1; col.8, lines 7-10). The reference disclosed that

the individual reservoirs are provided with differing permeable polymers to adapt the diffusion flow of the individual active ingredients to the respective need (col.5, lines 23-27). The reference disclosed method of making the system including the steps of mixing the hormone with the adhesive and the solvent, coating the mixture on the cover layer, drying the mixture and applying the removable protective layer, and finally laminating and punching the product to obtain the individual patches (col.4, lines 1-15; col.8, example 4).

US '394 does not teach the size of the space that separate the two matrices as claimed in claim 1.

The claimed size does not impart patentability to the claims, absent evidence to the contrary. However, the reference suggests that care must be taken for sufficient spacing of the areas to prevent a diffusion of active ingredient in the respective other area.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal therapeutic system comprising two adhesive matrices, one loaded with progesterone and the other loaded with estrogen as disclosed by US '394, and adjust the space between the two matrices to obtain independent delivery of the two hormones, motivated by the teaching of the reference that care must be taken for sufficient spacing of the areas to prevent a diffusion of active ingredient in the respective other area, with reasonable expectation of having transdermal therapeutic system that deliver progesterone and estrogen from two separate matrices to the patient in need of such treatment with success.

11. Claims 1-3, 5, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,538,736 ('736).

US '736 teaches an active substance containing plaster for controlled administration of active substances to the skin. The plaster comprises a backing layer, an active substance reservoir divided perpendicularly to the skin contact surface of the plaster and having one or more active substances, contact adhesive layer on the skin contact layer, and removable protective layer that is removed prior to application to the skin (abstract). The active substance reservoirs can contain estrogen and gestagen (col.3, lines 57-63). The active substance reservoirs are separated by a gap of 14 mm and are covered by adhesive layers (col.5, lines 1-50). The skin contact adhesive layer is made of silicone (col.8, line 63). The reference disclosed a method of production of the plaster comprising mixing the active substance, the solvent and the polymer, drying the mixture and laminating the product to the other layers (col.9, lines 1-41). The reference disclosed that the disclosed sizes are not intended to restrict the invention and can be adapted by the expert in the field to the therapeutic requirement and rational production (col.7, lines 48-55).

US '736 does not teach the size of the space that separate the two matrices as claimed in claim 1.

The claimed size does not impart patentability to the claims, absent evidence to the contrary. However, the reference suggests that care must be taken for sufficient

spacing of the areas to prevent a diffusion of active ingredient in the respective other area.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal therapeutic system comprising two drug containing reservoirs, one loaded with gestagen and the other loaded with estrogen as disclosed by US '736, and adjust the gap between the two reservoirs to obtain the desired delivery of the two hormones, motivated by the teaching of the reference that the disclosed sizes are not intended to restrict the invention and can be adapted by the expert in the field to the therapeutic requirement and rational production, with reasonable expectation of having transdermal therapeutic system that deliver gestagen and estrogen from two separate reservoirs to the patient in need of such treatment with success.

12. Claims 1-6, 9, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 5,296,230 ('230).

US '230 teaches a transdermal fertility control system comprising multi-region transdermal delivery dosage unit and method of its making (abstract). The dosage unit delivers different steroid hormones from different regions within a single dosage unit (col.16, lines 63-68). The different regions have different shapes (col.18, lines 66-68). The dosage unit contains the hormones in a matrix made of silicon adhesive polymer (col.3, lines 55-62). The reference discloses that factors can be changed to control the amount or ratio of hormones delivered from the system, and among these factors are

the area and area ratio of each region, and changing the type of polymer adhesive which forms each region (col.17, lines 16-23). Hormones to be delivered by the disclosed system is combination of 17beta-estradiol and progesterone, such as megestone (col.4, lines 6-7; col.12, lines 29-30). The references discloses method of making of the device comprising mixing the ingredient, drying them on backing and laminating the product to other layers (col.18, lines 9-60).

US '230 does not teach the size of the space that separate the two matrices as claimed in claim 1.

The claimed size does not impart patentability to the claims, absent evidence to the contrary. However, the reference suggests that care must be taken for sufficient spacing of the areas to prevent a diffusion of active ingredient in the respective other area.

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal therapeutic system comprising two regions to deliver megestone from one region and estradiol from the other as disclosed by US '230, and adjust the area between the two regions to obtain the desired delivery of the two hormones, motivated by the teaching of the reference that factors can be changed to control the amount or ratio of hormones delivered from the system, and among these factors are the area and area ratio of each region, with reasonable expectation of having transdermal therapeutic system that deliver megestone and estradiol from two separate regions to the patient in need of such treatment with success.

13. Claims 4 and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '931, US '394 and US '736 in view of US 5,834,452 ('452).

The teachings of the US '931, US '394 and US '736 are discussed above. However, the references do not teach the progesterone species trimegestone as claimed in claim 4. US '736 does not teach the estrogen species estradiol as claimed in claim 6.

US '452 teaches a composition that can be in the form of a patch comprises the progestomimetic compound trimegestone and the estrogen compound 17beta-estradiol, such a combination find use in hormonal replacement treatment relating to menopause and particularly in the prevention or treatment of osteoporosis (abstract; col.3, lines 12, 38-60; col.10, table in the bottom of col.10).

Thus, it would have been obvious to one having ordinary skill in the art at the time of the invention to provide a transdermal patch comprising two compartments to deliver progesterone and estrogen loaded into two separate compartments as disclosed by any of the US '931, US '394 and US '736, and to load one compartment with trimegestone and the other with estradiol, motivated by the teaching of US '452 that such a combination find use in hormonal replacement treatment relating to menopause and particularly in the prevention or treatment of osteoporosis, with reasonable expectation of success of the delivered patch to deliver patch comprising combination of estradiol and trimegestone provided in two separate compartments to treat patient in need with success.

14. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over any of US '931, US '394 and US '736 in view of US '452 as applied to claims 1-6, 9 and 10 above, and further in view of WO93/10772 ('772).

The teachings of the references in combination are discussed above. However, the references do not teach the species of the acrylate used with the estradiol to be 2-ethylhexyl acrylate and vinyl acetate copolymer.

WO '772 teaches transdermal delivery system to deliver 17beta-estradiol to the skin said system comprises the drug in 2-ethylhexyl acrylate and vinyl acetate copolymer matrix (abstract). The system is well-tolerated, stable, effective, prevents crystallization of the drug and ensures adequate extended level of active ingredient in the blood and has good tack and adhesive properties (paragraph bridging page 5 and 6).

Thus, it would have been obvious to one having ordinary skill in the art a the time of the invention to provide a transdermal drug delivery device to deliver trimegestone and 17beta-estradiol as disclosed by the combination of the above references, and select 2-ethylhexyl acrylate and vinyl acetate copolymer matrix to deliver the estradiol, motivated by the teaching of WO '772 that the 2-ethylhexyl acrylate and vinyl acetate copolymer matrix is well tolerated, stable, effective, prevents crystallization of estradiol and ensures adequate extended level of the hormone in the blood and has good tack and adhesive properties, with reasonable expectation of the delivered device to provide the combination of hormones from two different matrices with success.

15. Claims 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over US '230 in view of WO '772.

The teachings of US '230 are discussed above. However, the reference does not teach the species of the acrylate used with the estradiol to be 2-ethylhexyl acrylate and vinyl acetate copolymer.

WO '772 teaches transdermal delivery system to deliver 17beta-estradiol to the skin said system comprises the drug in 2-ethylhexyl acrylate and vinyl acetate copolymer matrix (abstract). The system is well-tolerated, stable, effective, prevents crystallization of the drug and ensures adequate extended level of active ingredient in the blood and has good tack and adhesive properties (paragraph bridging page 5 and 6).

Thus, it would have been obvious to one having ordinary skill in the art a the time of the invention to provide a transdermal drug delivery device to deliver megestone and 17beta-estradiol from two different regions as disclosed by US '230, and select 2-ethylhexyl acrylate and vinyl acetate copolymer matrix to deliver the estradiol because US '230 disclosed that factors can be changed to control the amount or ratio of hormones delivered from the system, and among these factors are changing the type of polymer adhesive which forms each region, and further motivated by teaching of WO '772 that the 2-ethylhexyl acrylate and vinyl acetate copolymer matrix is well tolerated, stable, effective, prevents crystallization of estradiol and ensures adequate extended level of the hormone in the blood and has good tack and adhesive properties, with

reasonable expectation of the delivered device to provide the combination of hormones from two different matrices with success.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Isis Ghali whose telephone number is (571) 272-0595. The examiner can normally be reached on Monday-Thursday, 7:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman Page can be reached on (571) 272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Isis Ghali
Examiner
Art Unit 1615

IG

Isis Ghali

ISIS GHALI
PATENT EXAMINER